

TOUGH DECISIONS: TRANSPLANT, MECHANICAL SUPPORT OR PALLIATIVE CARE

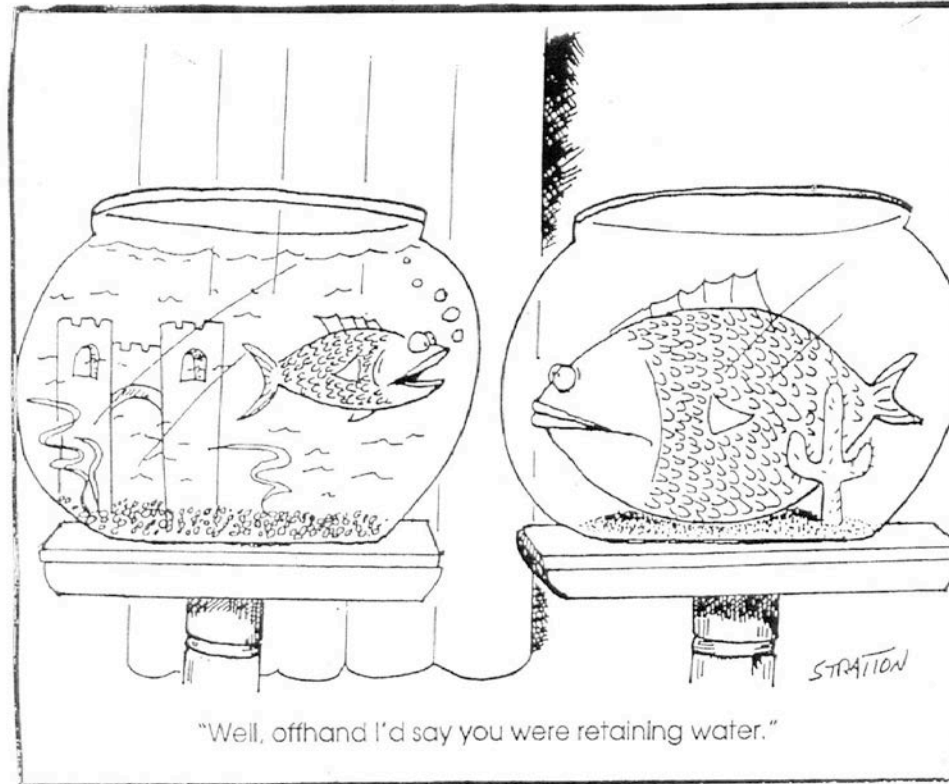
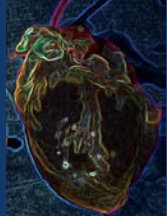
SAVITRI FEDSON, MA, MD
SEPTEMBER 16, 2016



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***“The very essence of cardiovascular practice is
the early detection of heart failure”***
Sir Thomas Lewis, 1933

I have no relevant financial disclosures or conflicts

I will not be discussing off label use of pharmaceutical agents or devices



Objectives

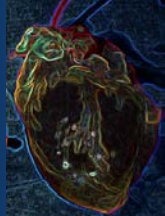
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To discuss available treatment strategies for advanced cardiothoracic disease

To discuss patient factors that effect these options



What is Heart Failure

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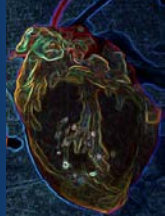


A clinical syndrome of sodium and water retention leading to breathlessness caused by neurohormonal activation in the setting of cardiac disease

No reference to ejection fraction or systolic function
Nothing about etiology

Symptoms result from:

- Increased filling pressures with relaxation
- Inadequate rise cardiac output with exercise
- Reduced resting cardiac output



Burden of Heart Failure



Annually in US

Prevalence	Incidence	Primary Mortality	Hospital admissions	Re-Hospital <30d	Cost
5,100,000	>650,000	55,000	>1,000,000	25%	\$39 billion

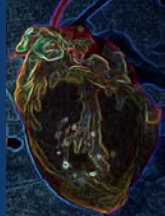
50% of people who have heart failure die within 5 years of diagnosis

200,000 people have Stage D HF with >70% annual mortality

It is the leading cause of hospitalization for those >65 yo with a 22% annual mortality following the first hospitalization

Death is 6-9x more common than general population

Mortality greater than AIDS, lung, prostate and breast cancer combined



What is in a Name?



Heart failure (preferred over congestive heart failure)

Symptoms of dyspnea and fatigue

Inability to meet the metabolic demands of the body, or having to do so with elevated filling pressures

EF (%)	EF ≤ 40	41-49	≥ 50
	HFrEF		HFpEF
		HFpEF borderline	
		HFpEF improved (from HFrEF)	

Preserved LVEF (cut off has varied from LVEF 40-55%; normal LVEF=>=55%)

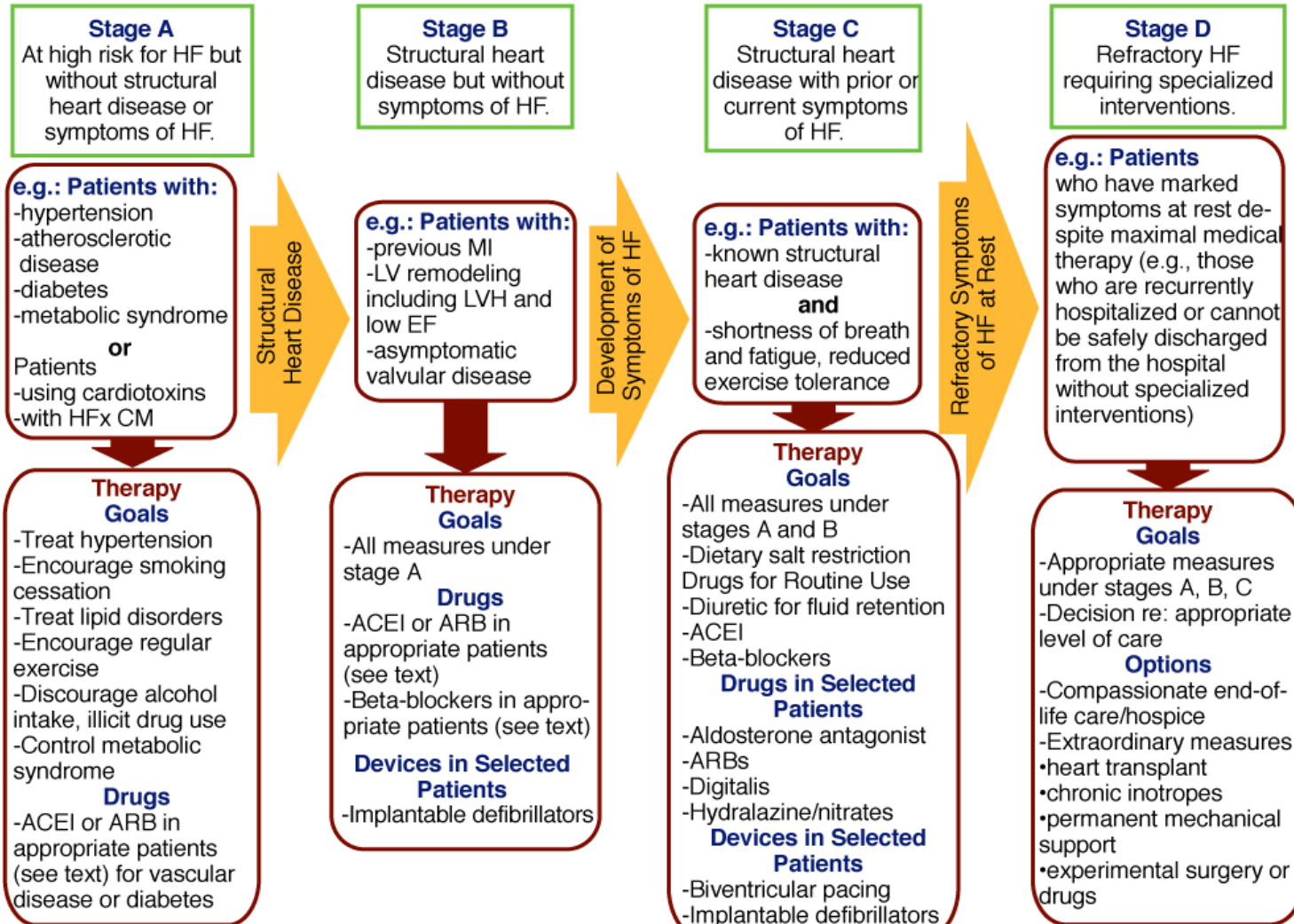
Absence of significant valvular, pericardial and ischemic heart disease

ACC/AHA HF Stages



At Risk for Heart Failure

Heart Failure

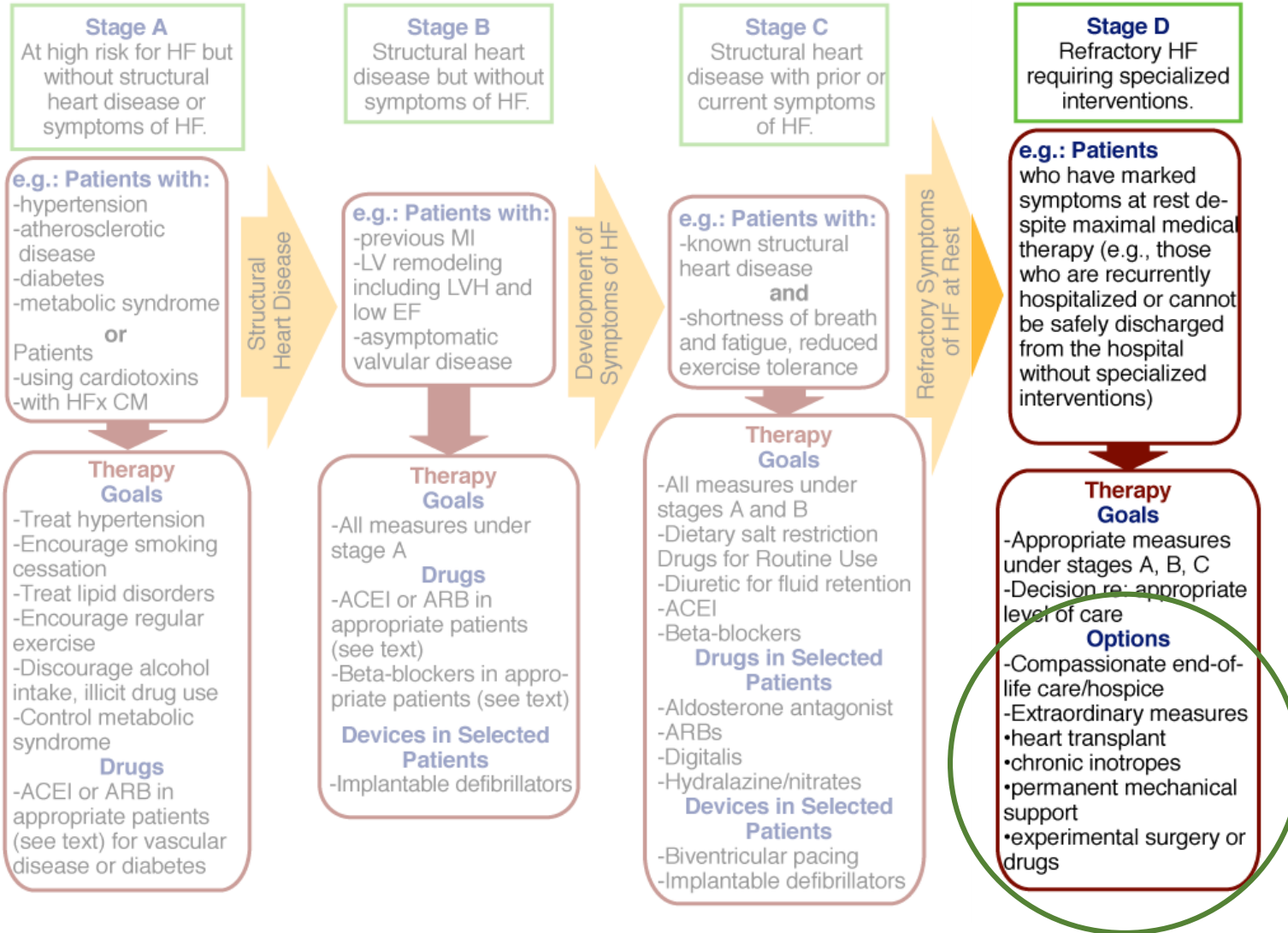


ACC/AHA HF Stages



At Risk for Heart Failure

Heart Failure





NYHA Functional Classification

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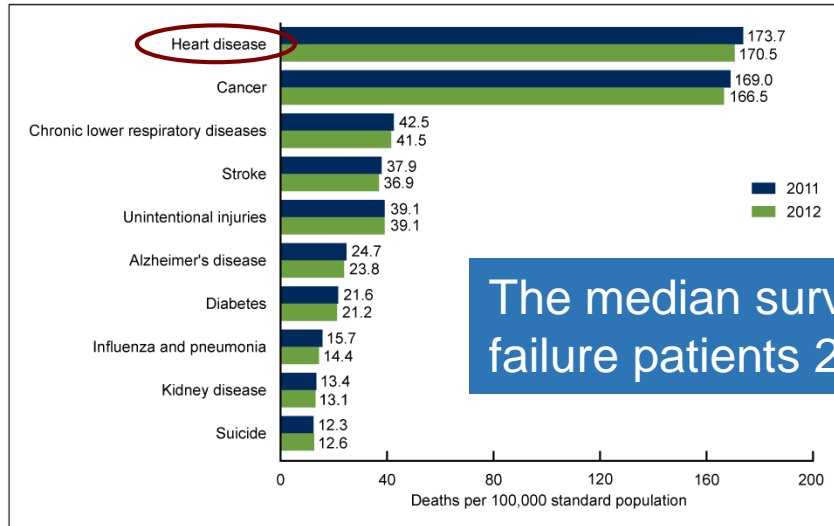


- Class I:** No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or angina.
- Class II:** Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
- Class III:** Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in fatigue, palpitation, dyspnea, or angina.
- Class IV:** Unable to carry on any physical activity without discomfort. Symptoms present at rest. With any physical activity, symptoms increase.

Advanced HF– Stage D



Figure 3. Age-adjusted death rates for the 10 leading causes of death in 2012: United States, 2011–2012



The median survival for heart failure patients 2.1 years

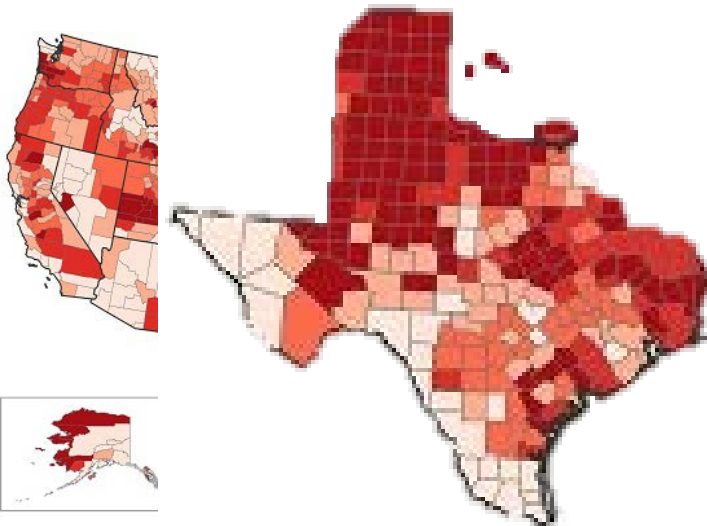
Refractory HF requiring specialized interventions

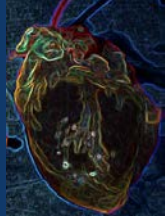
Patients who have marked symptoms at rest despite maximal medical therapy

All medical therapies AND Mechanical assist devices, Heart Transplantation, Continuous IV inotropic infusions for palliation Hospice

NOTE: Access data table for Figure 3 at: http://www.cdc.gov/nchs/data/databriefs/db168_table.pdf#1.
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality.

1-13

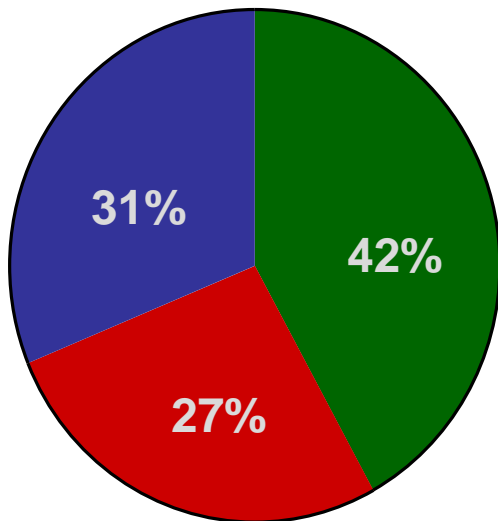




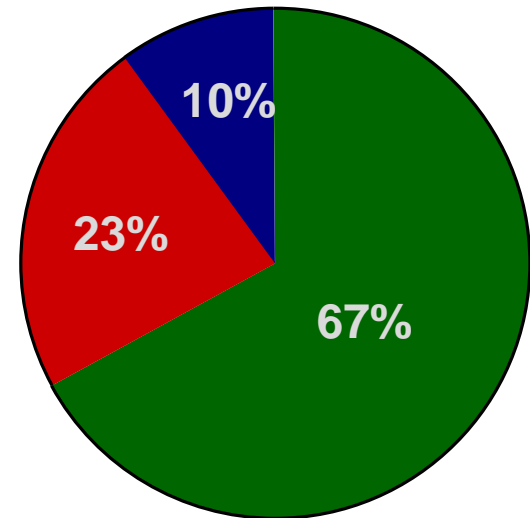
Function with HF > 65 Years



Men

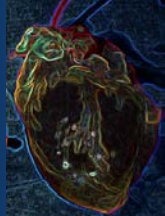


Women



- Normal EF
- Borderline EF
- Reduced EF

Cardiovascular Health Study



Etiology of HF



Ischemic heart disease

Hypertension

Valvular heart disease

Cardiomyopathies

Dilated

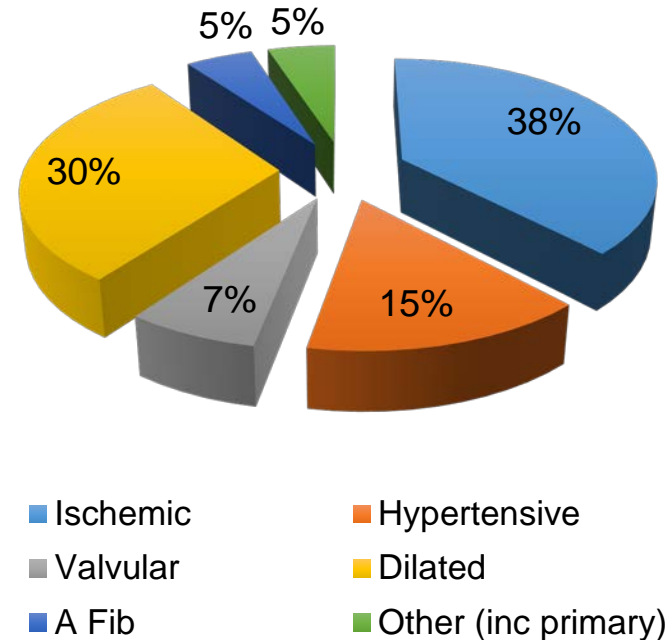
Arrhythmic (typically
tachycardia)

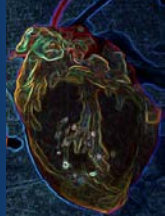
Familial

Congenital heart disease

Risks also:

Alcohol, obesity, diabetes, thyroid
disease, infections





Heart Failure

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Patients with HF often do not understand their disease prognosis

Cognitive deficits - affect the ability to understand and self manage

Comorbidities contribute, cardiorenal, hepatic congestion, encephalopathy

Defects are in functional domains – visual- spatial, insight

There is often no clearly defined terminal phase to direct conversations

Survival time vs. quality of life

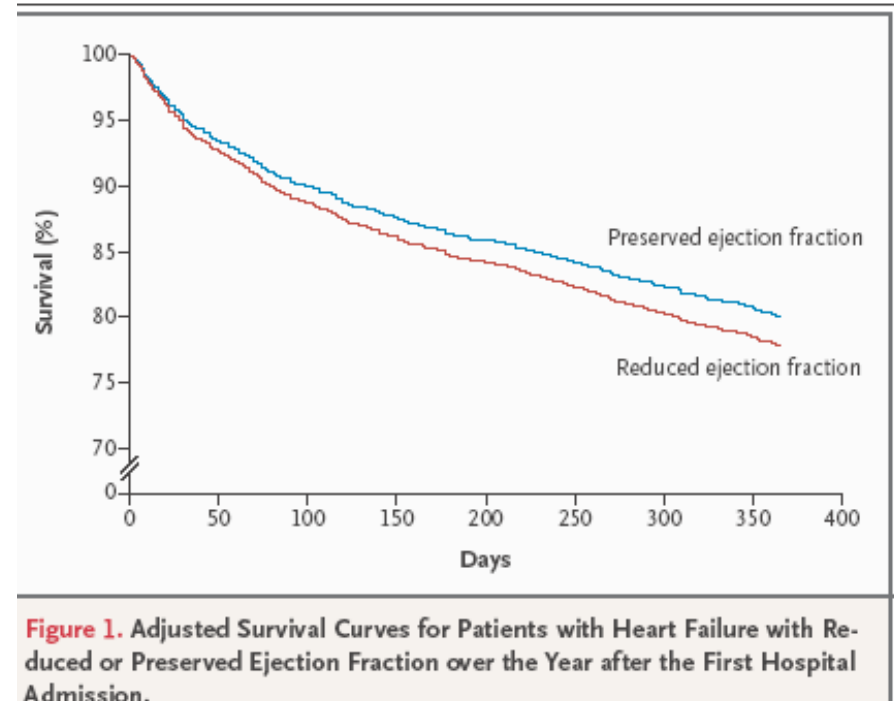
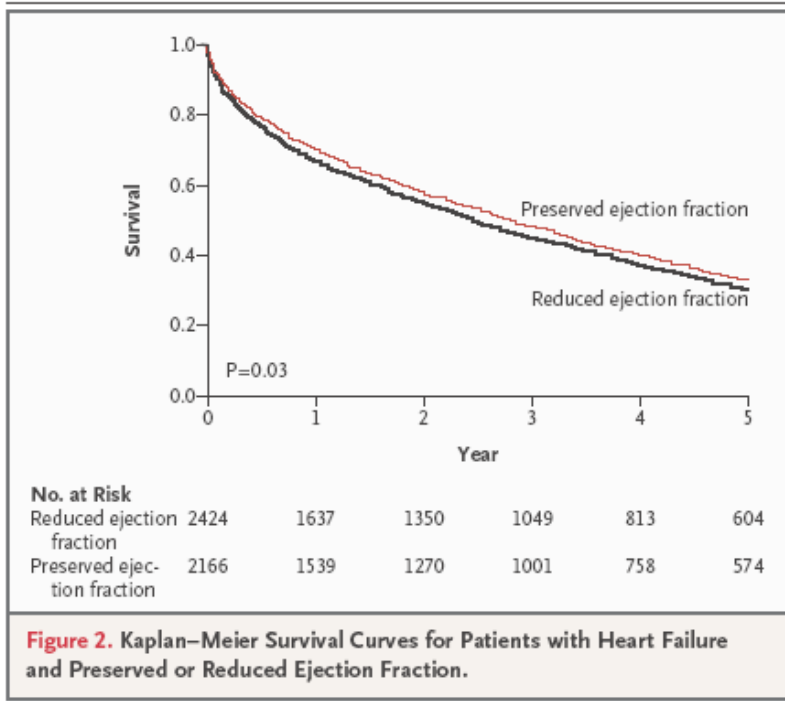
Time to prepare for things, get affairs in order

MacIver et al. JLHT 27:2008
Murks, CM, Fedson SF – unpublished data

Lewis et al. JHLT 2001

Kirkpatrick et al. Am J Geriatr Med 2007

Survival Differences: EF



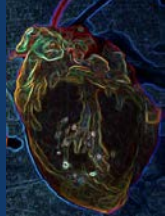
Worse survival associated with lower EF, renal dysfunction, hospital admission

Systolic
HFrEF

EF < 40%
Contractile dysfunction

“Diastolic”
HFpEF

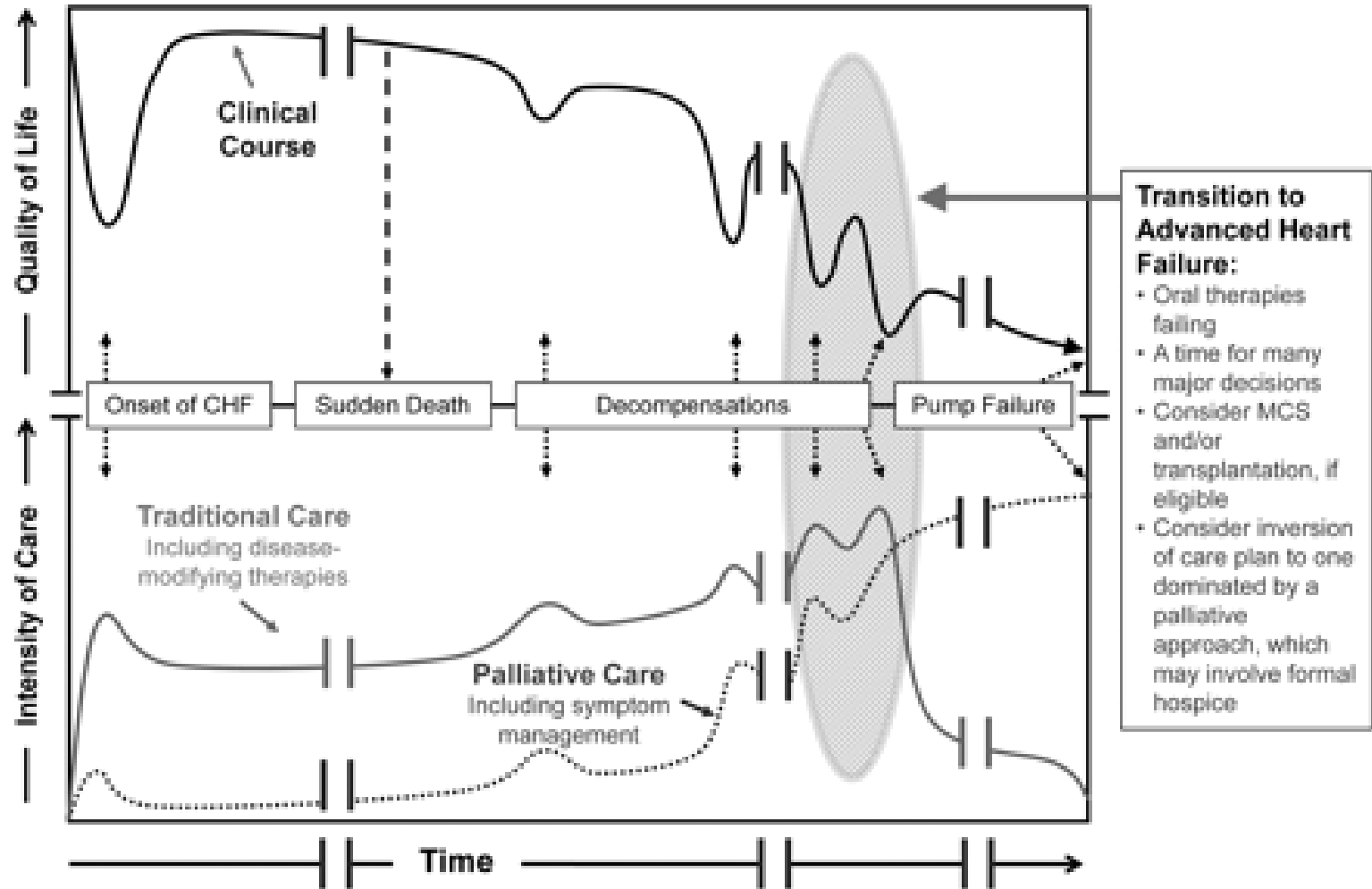
EF >40%
Relaxation/compliance dysfunction



Trajectory of (systolic) Heart Failure

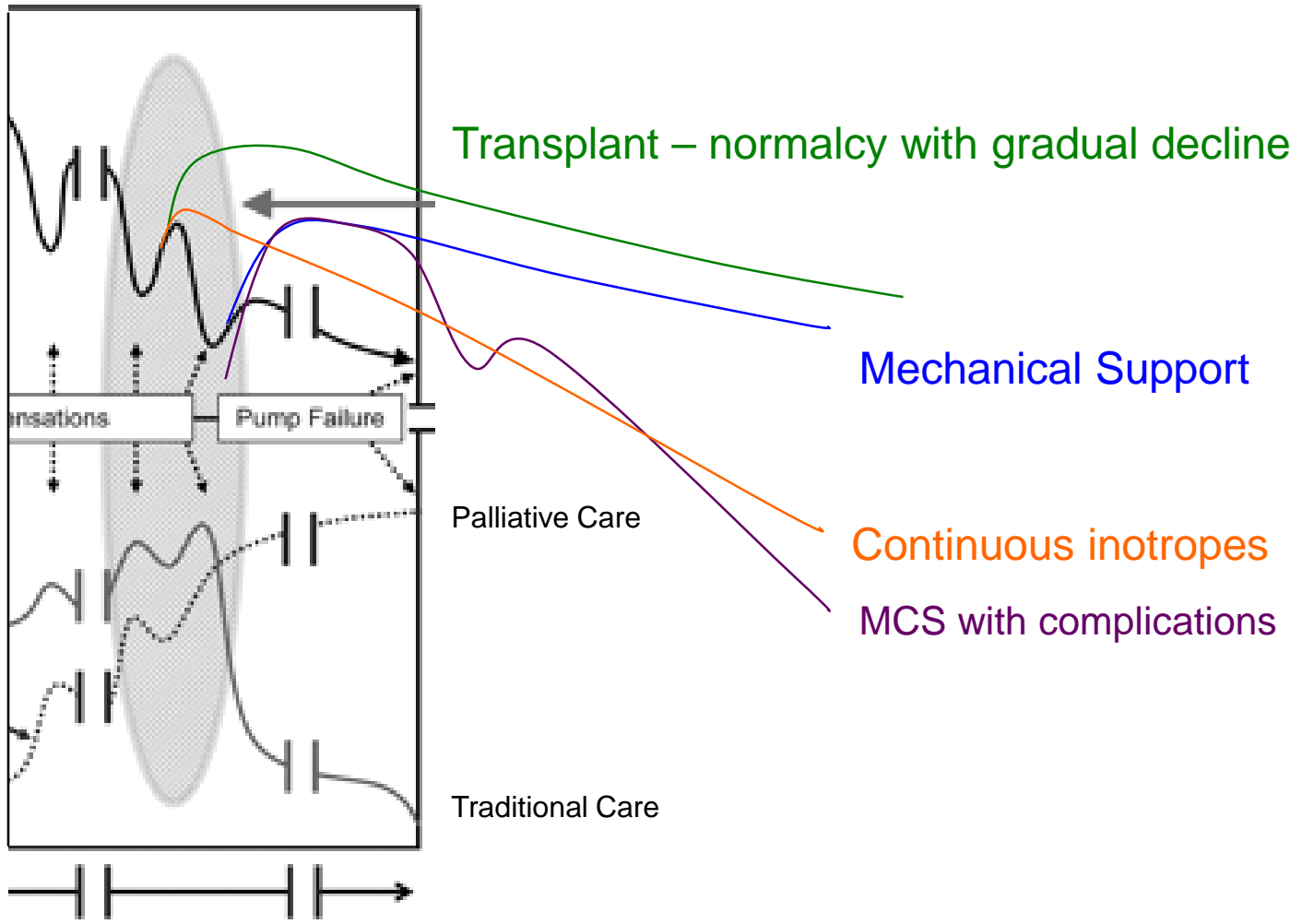
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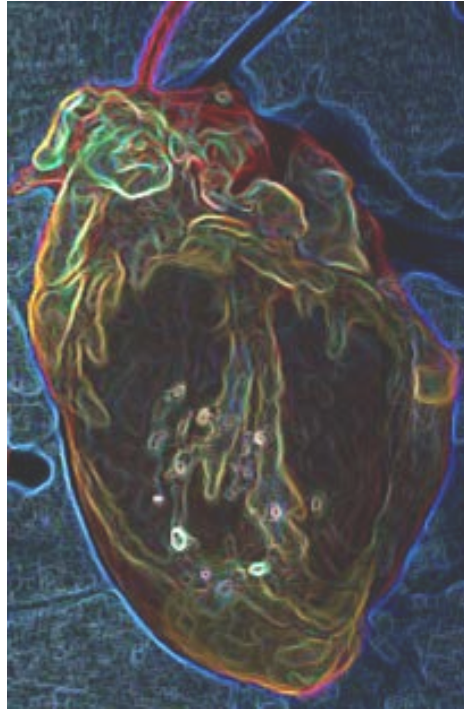
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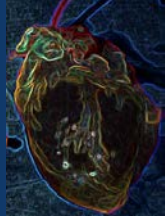


Trajectory of (systolic) Heart Failure





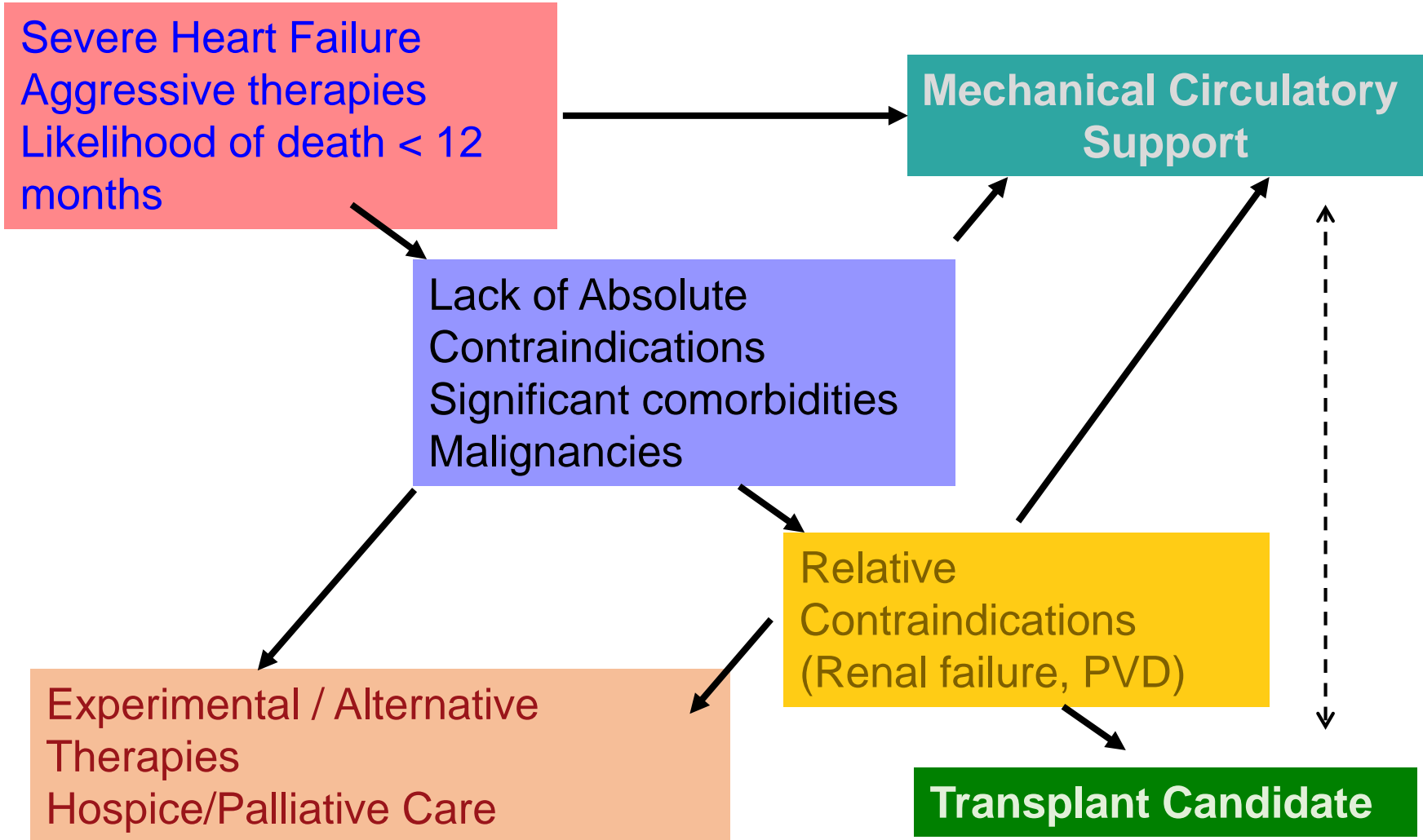
OPTIONS FOR STAGE D



Therapeutic Options Stage D

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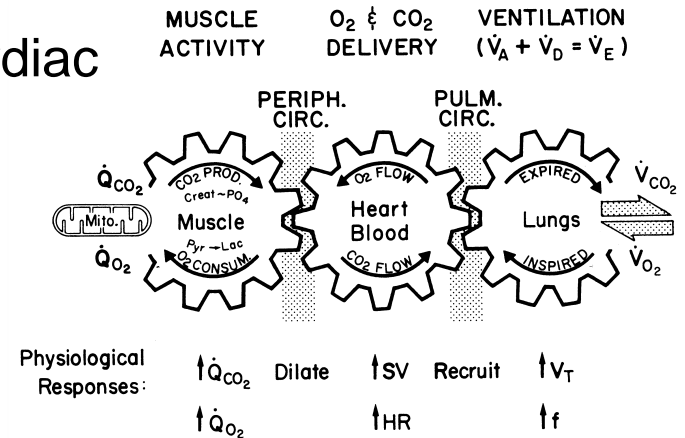
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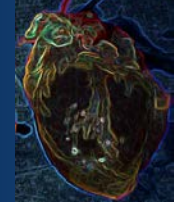
Cardiopulmonary stress testing



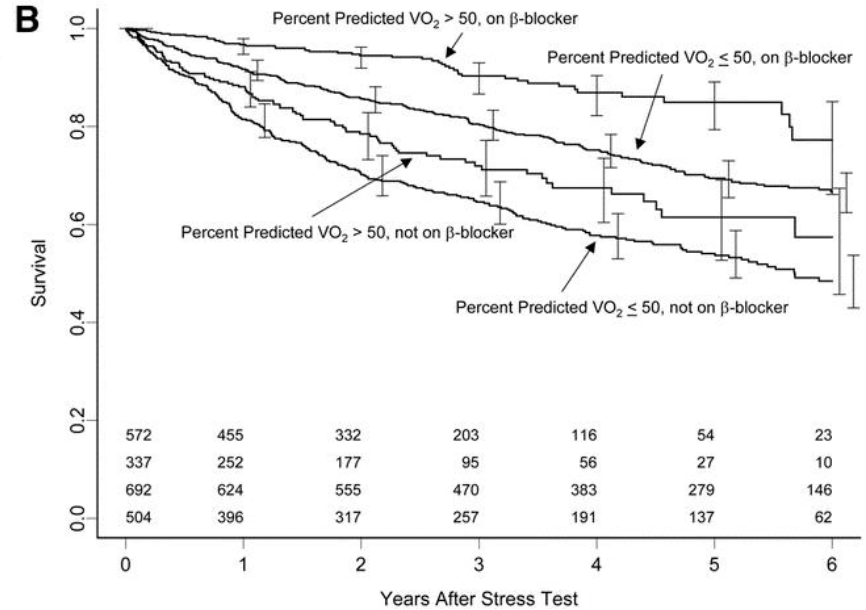
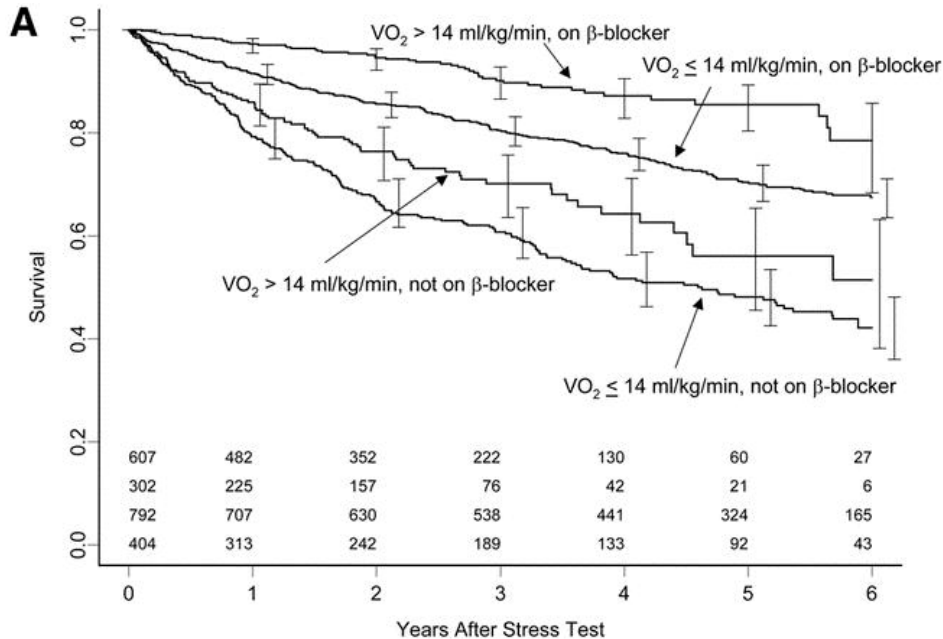
Invasive/non invasive measurement of Cardiac Output – poor predictors of symptoms, exercise capacity, prognosis and need for transplantation



Study	pVO ₂ (ml/kg/min)	Outcomes (mortality)
Mancini et al Circ 1991	< 14 candidate for OHT <14 not candidate for OHT >14 too well for OHT	52% 1 yr 68 % 2 yr 16 % 2 year
Szlachcic et al AJC 1985	<10 >10	77% 1 yr 21% 1 yr
Likoff et al AJC 1987	<13 >13	64% 1 yr 85% 1 yr
Stelken et al JACC 1996	≤ 50% predicted > 50% predicted	26% 1 yr, 57% 2 yr 2% 1yr, 10% 2 yr



CPET – $\beta\beta$ and VE/VCO_2



All cause mortality
Peak O₂ still discriminatory
Consider different cut-point – given improved survival with beta blockers (12ml/kg/min)

Excessive ventilatory response (ie VE/VCO_2 slope of ≥ 35) = mortality rate similar to peak VO_2 of ≤ 10 ml/kg/min (whole population)



Right Heart Hemodynamics

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PA Hypertension, PVR

Predictive for morbidity and eligibility in Transplant AND LVAD

Response to vasodilator therapy (transplant)

PCWP < 16mmHg – 83 % 1yr survival 83% v. 38% without response to vasodilator testing

Donor RV does not tolerate PASP 55-60mmHg

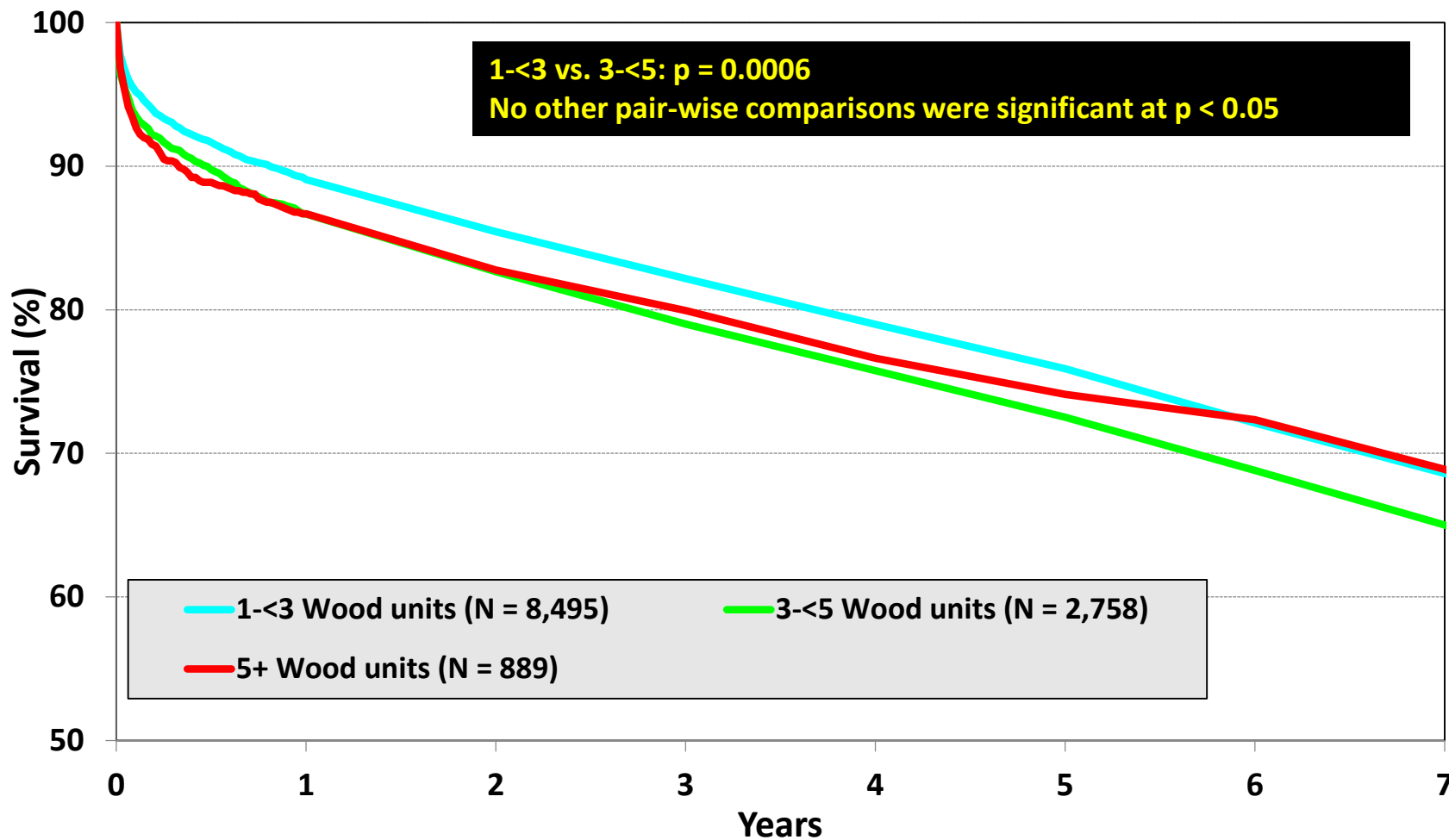
RV failure, graft dysfunction, death

Much PA HTN is reactive, or secondary to elevated PCWP

Vasodilator testing for responsiveness – residual PVR of 2.5 WU increases transplant mortality



Transplant Survival by PVR (Tx 1/03 – 6/11)



RV Failure post LVAD



	AUC (95% CI)	*p Value
RV failure risk score	0.73 (0.65–0.81)	—
Severe RV failure on echocardiograph	0.59 (0.51–0.68)	0.004
RVSWI	0.63 (0.55–0.72)	0.011
PVR	0.50 (0.41–0.59)	<0.001
TPG	0.56 (0.48–0.65)	<0.001
PA systolic pressure	0.59 (0.51–0.68)	0.017
RA pressure	0.53 (0.44–0.61)	<0.001

CVP:PCWP >0.63

PAC = SV/PASP-PADP

PASP-PADP/CVP = PAPI

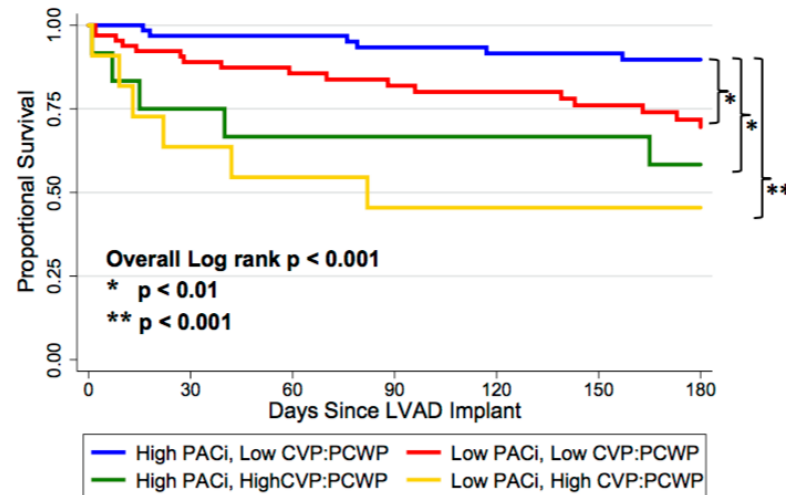


Figure 3 Kaplan–Meier curves for 6-month survival stratified by a hemodynamic profile of indexed pulmonary arterial compliance (PACi) and the ratio of central venous pressure to pulmonary capillary wedge pressure (CVP:PCWP).



Transplant (and LVAD) Evaluation

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Look for co-morbidities that effect survival and quality of life

Pulmonary limitation – O2 dependence, - PFTs

Vascular disease (cerebral, arterial) – Carotid duplex, ABI, Eval for AAA

Infectious Disease –

- HIV – relative contraindication
- Hep B/C – relative without OLT
- EBV – risk for PTLD
- CMV – risk for primary, reactivation
- TB – risk for reactivation
- RPR – needs treatment

Renal Disease –

- Risk for renal failure
- SPEP/UPEP in addition

Dental – abscess, oral lesions (cancer)

Anticipated risks/needs –
Homocysteine, G6PD

Cancer Screening –

- Age and risk appropriate
- Colonoscopy
- PSA
- Mammography
- PAP
- High Res CT for smokers



Indications for LVAD

Class IV heart failure unresponsive to Optimal Medical Management for at least 60 of last 90 days

LVEF < 25%

Functional limitation VO₂ <12 ml/kg/min, or inotrope dependence

Appropriate size (BSA 1.5m²)

Intention:

Destination Therapy (DT)

Bridge to ... Transplantation (BTT)

Type:

Durable – longevity, ambulatory

Temporary – months of support, +/- ambulatory, often only in hospital

LVADs are restorative –
not reversing the course of heart failure
changing the trajectory of demise and symptoms
(similar to hemodialysis)

They are also life sustaining and life prolonging at times



Candidacy – for Options

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TRANSPLANT

$VO_2 \leq 14$ ml/kg/min (12 on $\beta\beta$)

Age ≤ 70 years

BMI ≤ 35 kg/m²

Cancer – if likelihood of recurrence is low, negative metastatic work up (No time period stated)

No significant other co morbidities that are not managed (renal ftn, diabetes)

Appropriate psychosocial evaluation – no substance abuse

LVAD

Class IV HF unresponsive to OMM for at least 60 of last 90 days

LVEF $< 25\%$

Functional limitation $VO_2 < 12$ ml/kg/min, or inotrope dependence

Appropriate size (BSA 1.5m²)



Psychosocial Evaluation

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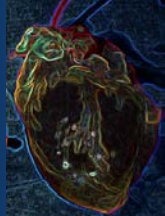
Often overlooked in the setting of complex medical diseases

Cognitive dysfunction in HF patients

Need to assess ability of patient to care for/manage transplant,
medical adjustments

Depression/substance abuse

PTSD (present in up to 11% of transplant candidates related to
ICD shocks)



Smoking and Transplantation

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Effects medical outcome

Thoracic selection criteria uses personal behaviors, compliance, alcohol, drug use, morbid obesity more than abdominal selection committees

Consequence of tobacco/marijuana use

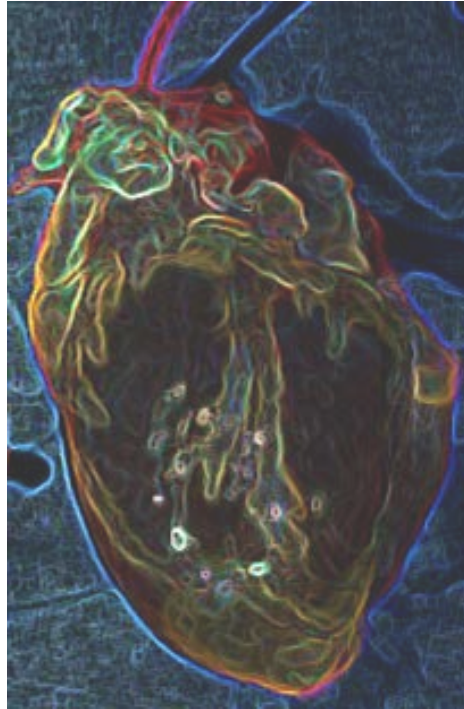
Medical outcomes of malignancy, all cause mortality

Patient's right to self-injurious behaviors

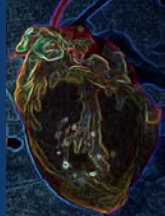
“Sin tax”

Is nicotine addiction a medical condition that warrants treatment?





Which Choice, What Patient



Transplant Numbers

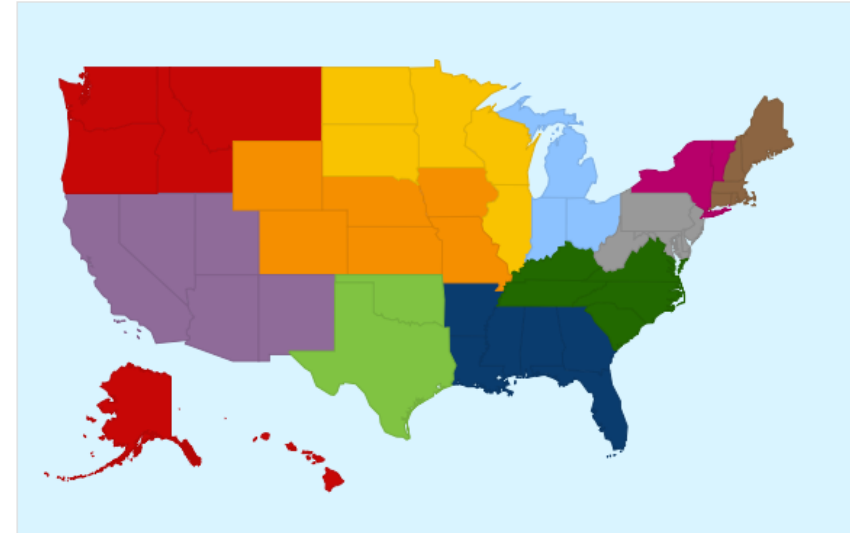
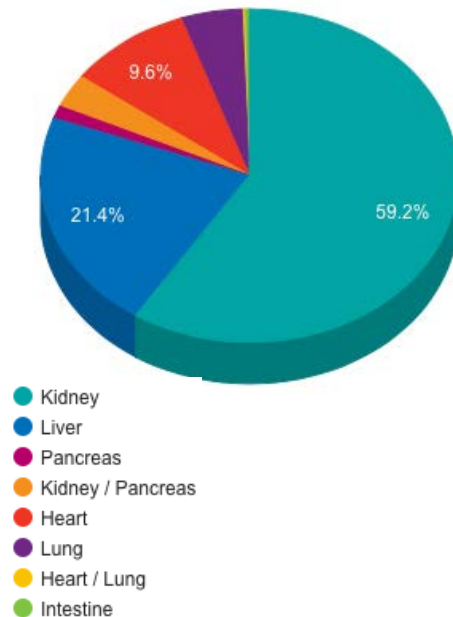


Waiting list 121,422
Active waiting 78,002

Jan-Nov 2015
Total transplants 28,211
Donors 13,708

Transplants Jan 1, 1988-Nov 30, 2015

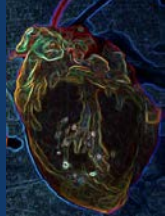
Organ	Transplants
Kidney	384,691
Liver	139,371
Pancreas	8,110
Kidney / Pancreas	21,262
Heart	62,267
Lung	30,822
Heart / Lung	1,181
Intestine	2,644
Total	650,348



Puerto Rico (Region 3) | Washington, DC (Region 2)

Learn more about each region:

- Region 1
- Region 5
- Region 9
- Region 2
- Region 6
- Region 10
- Region 3
- Region 7
- Region 11
- Region 4
- Region 8



Equity



Fairness/Impartiality

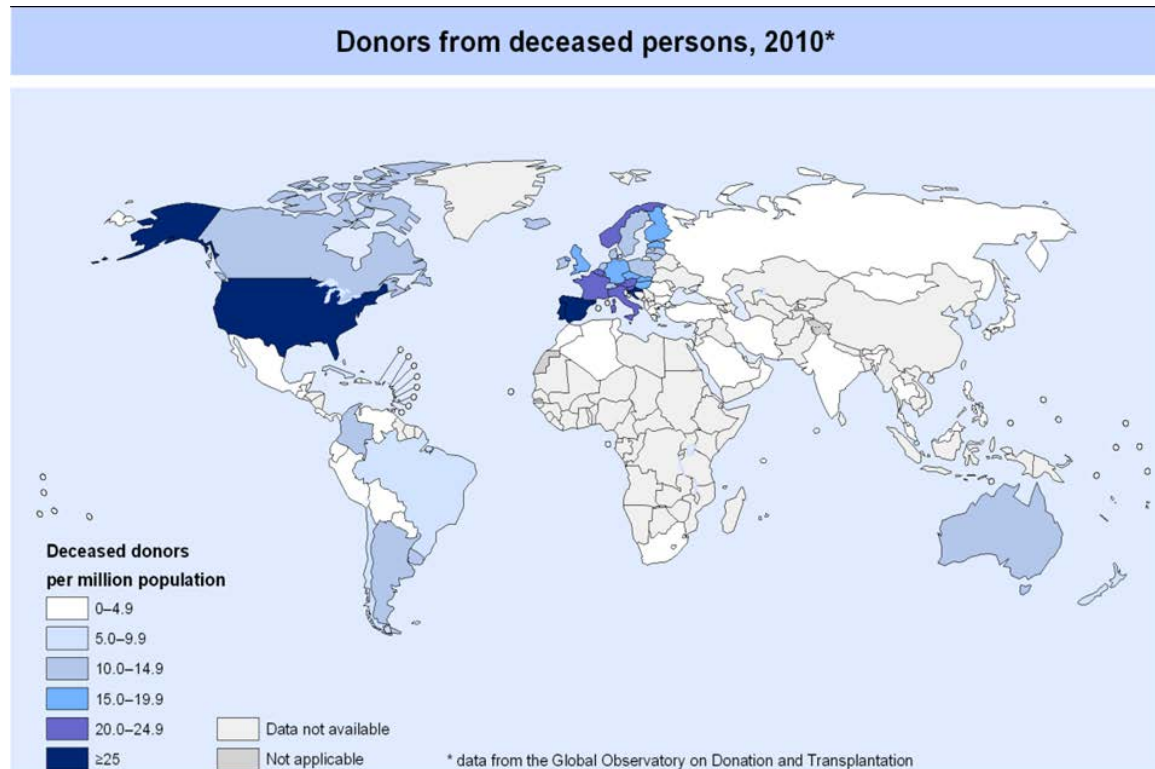
Access to transplant centers (listing at multiple centers)

Geographic – local, regional or national (country)

Physician ignorance

Insurance contracts

freedom from bias



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Observatory on Donation & Transplantation. Map Production: Public Health Information and Geographic Information Systems (GIS), World Health Organization



Which Choice, What Patient

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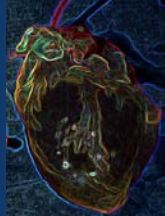
Medical considerations – the patient (candidate)
Not everyone is a transplant or MCS candidate

Cancer – moving target on issues of prostate cancer, non-melanomatous skin cancers

Age – how old is too old?
Physiologic age

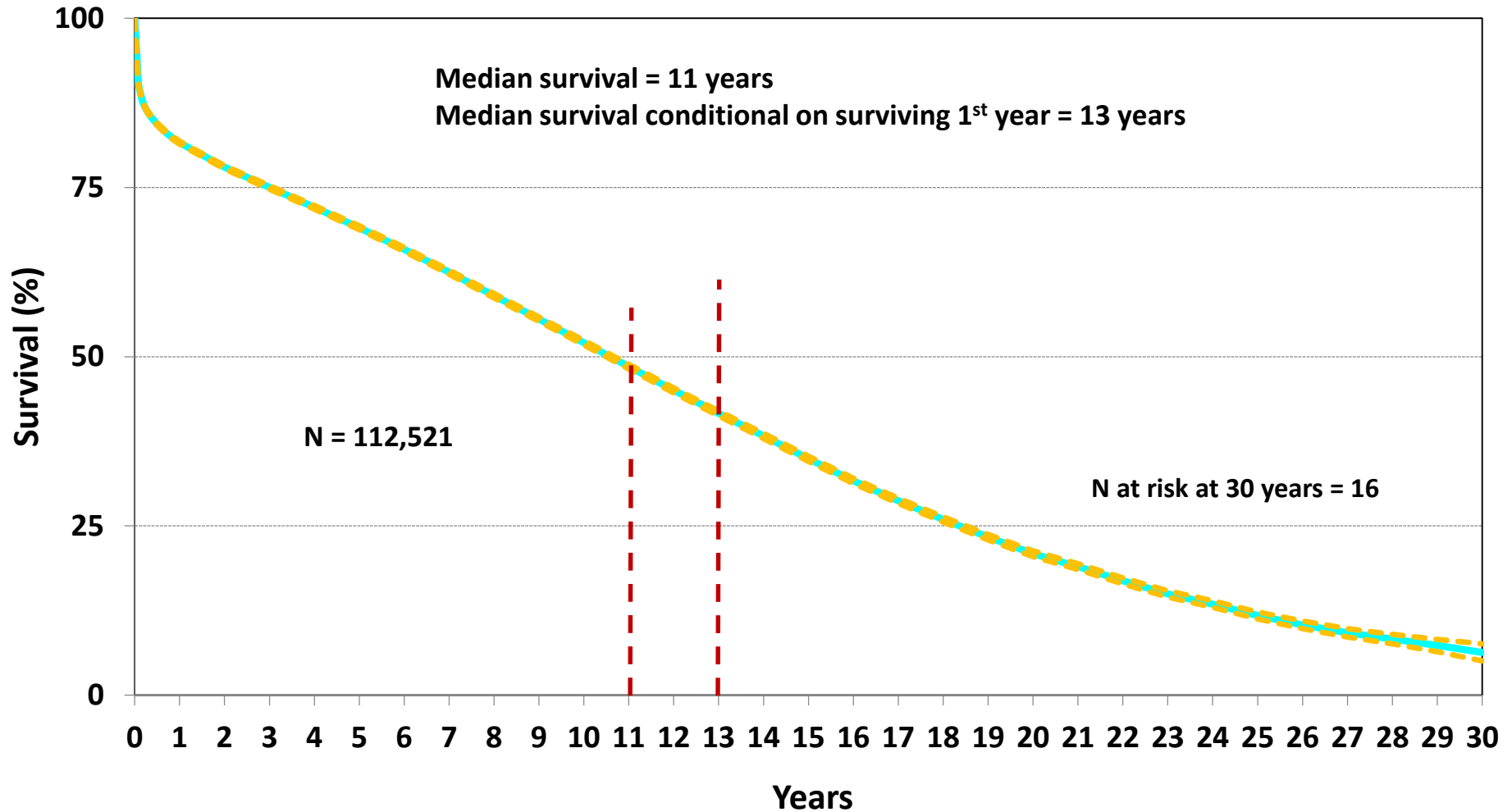
Mechanical Circulatory support – anticipated complications
Organic brain disease, infections
Colonic, Urologic pathology
RV function

Who can best use an organ or pump? Potential?



Heart Transplant Survival

(1/1982 – 6/2013)





Which Choice, What Patient

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Autonomy of persons is the ethical basis for consent
HF – cognitive impairment, (even when on VAD)

Exchange of one set of medical problems for another
DM, infection, PTLD and other cancers
Bleeding, CVA, infection, life with a “toaster”
Increase arrhythmia, less dyspnea

Primary of First Person consent – as distinguished from
surrogate decision making/ or substituted judgment for MCS



Which Choice, What Patient

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Can you submit patients to life shortening drugs for non-life extending transplantation?

What will MCS outcomes need to be?

Should age be considered in outcome expectations?

Are transplants going to be the option for those who cannot have a VAD?

Palliative inotropes



Sensitized Patients



Occurs from interaction of host (recipient) with non-self antigens

Previous transplant (most robust way of exposure to antigens)

Pregnancy (especially multiple paternity)

Blood transfusions – PRBC, pooled products, platelets

Composite tissue (congenital repairs, bioprosthetic valves)

Mechanical circulatory support (LVADs) – membrane exposure

Additional Risks

Hemodialysis

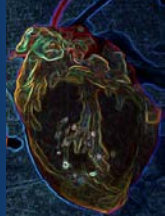
Viral infections (CMV)

Panel Reactive antibody (**PRA**) - % of cells from a panel of random donor against which a recipients serum reacts

>10% = sensitized

>80% = highly sensitized

>30% may necessitate aggressive desensitization protocols

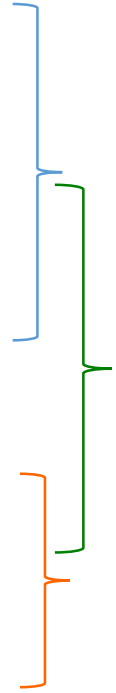


Intermacs



Interagency Registry for Mechanically Assisted Circulatory Support

Level	Clinical Status	Colloquially	Expected survival
1	Critical Cardiogenic Shock	<i>Crash and Burn</i>	<i>hours</i>
2	Progressive decline on Inotropes	<i>Sliding on inotropes</i>	<i>1-7 days</i>
3	Stable, inotrope dependant	<i>Dependant Stability</i>	<i>weeks</i>
4	Resting symptoms on Oral therapy	<i>Frequent flyer</i>	<i>Weeks to few months</i>
5	Exertion intolerant	<i>Housebound</i>	<i>Weeks to months</i>
6	Exertion limited	<i>Walking wounded</i>	<i>months</i>
7	Advanced NYHA III(b)		



Ideal implantation is INTERMACS 3-5

Ventricular Assist Devices

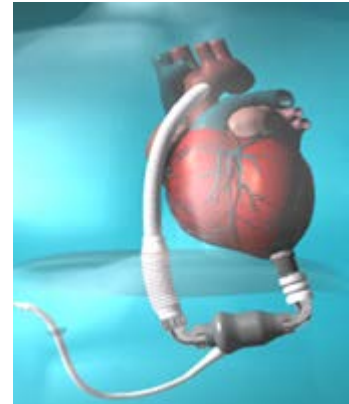


VAD implantable device

Decreased cardiac workload

Increases systemic circulation and tissue perfusion

Decreases Preload

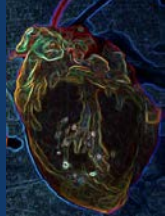


left (LVAD), right (RVAD) ventricle, or both (BiVAD)

External driveline to battery/comptroller

Electrical power 24 hours

No MRI, no Swimming



Good, Bad (Life with an LVAD)



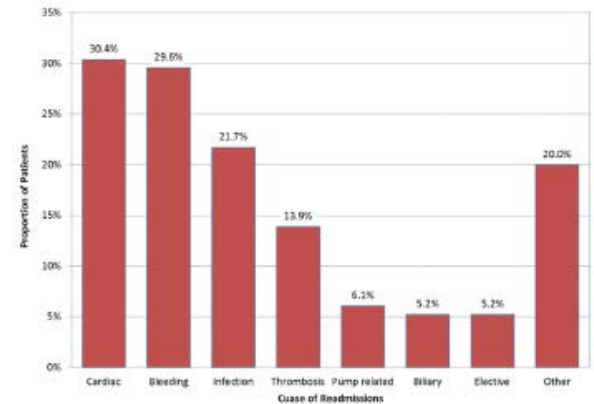
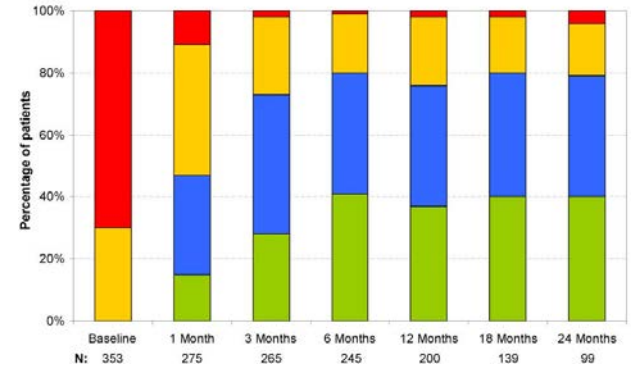
LVAD opportunity for “restoring life”

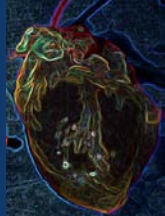
Improvement in multiple measures of quality of life – 6MWT, KCCQ, NYHA

Fewer than 50% of VAD implanted as a Bridge are transplanted

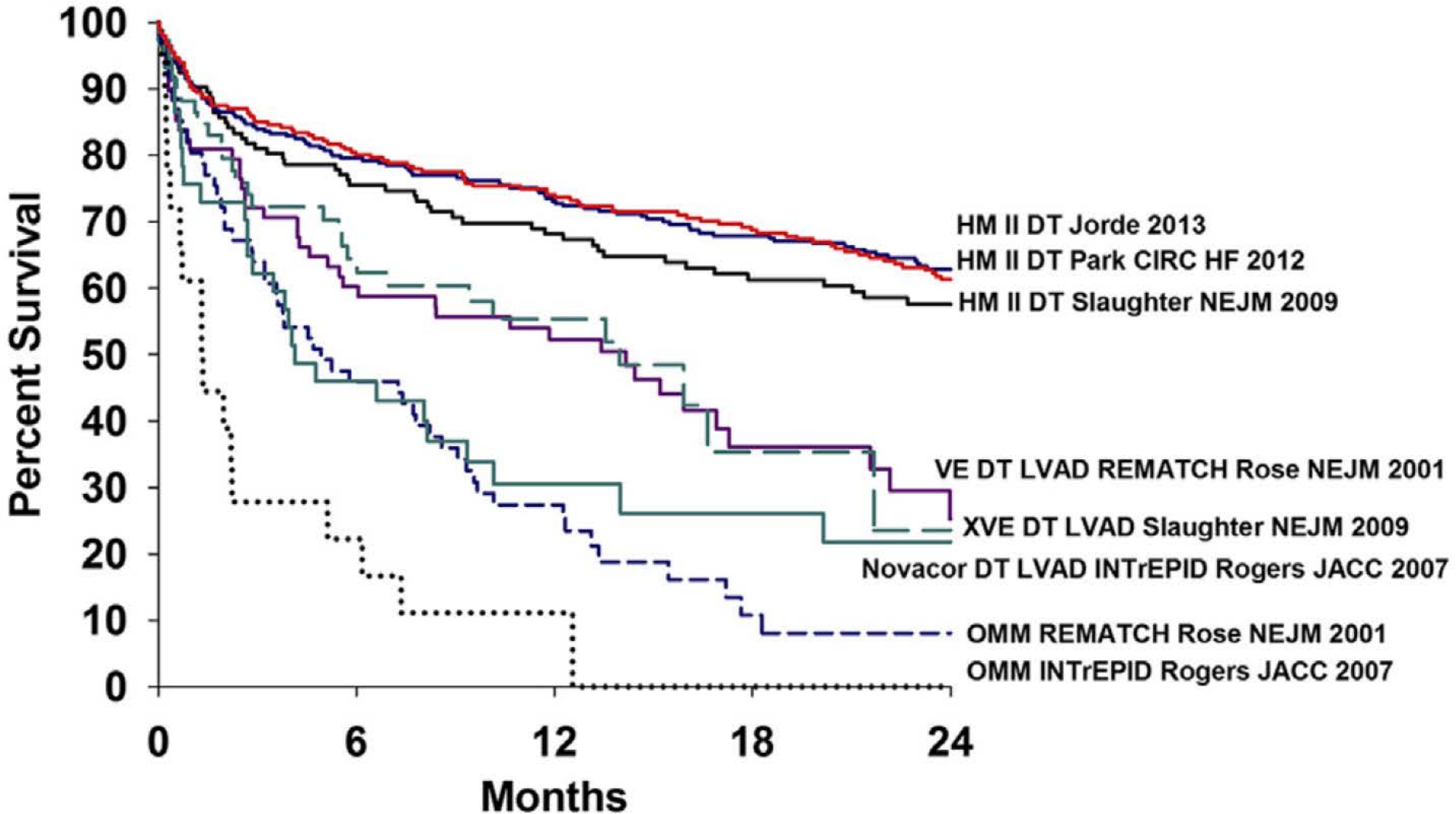
Bleeding – intracranial, GI, epistaxis, GU
 Thrombosis of LVAD
 Hemolysis
 Infections – driveline
 infections, bacteremia
 Recurrent Heart failure (RV failure)

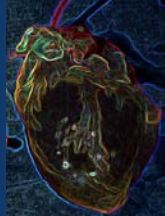
Destination





LVAD Survival





Palliative Options

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Palliative care –organized system of treatments to reduce symptoms of disease rather than alter prognosis

Applicable to anyone with a life-limiting or life-style limiting illness at any stage

Emphasis on Quality of Life

Based on NEED rather than prognosis or life-expectancy

The technology of LVADs can improve the “short wretched lives” of patients as a palliative option for destination patients

Destination Therapy has great potential for palliation

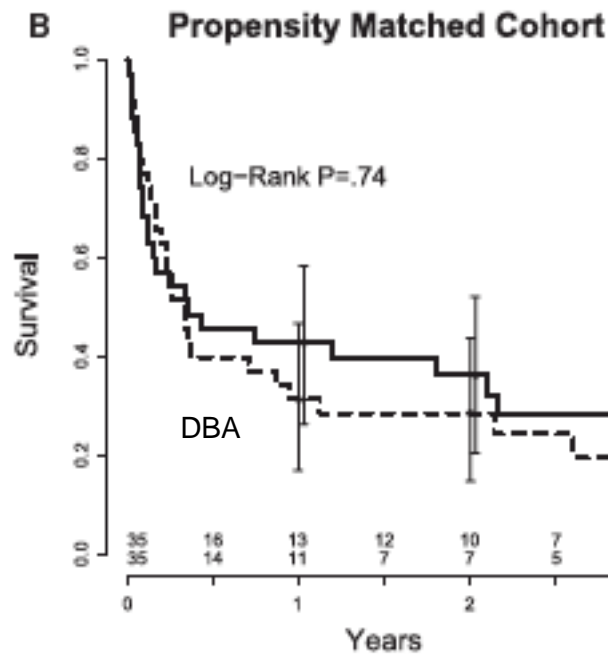
Also with great potential for complications with extreme morbidity and mortality

Inotropes

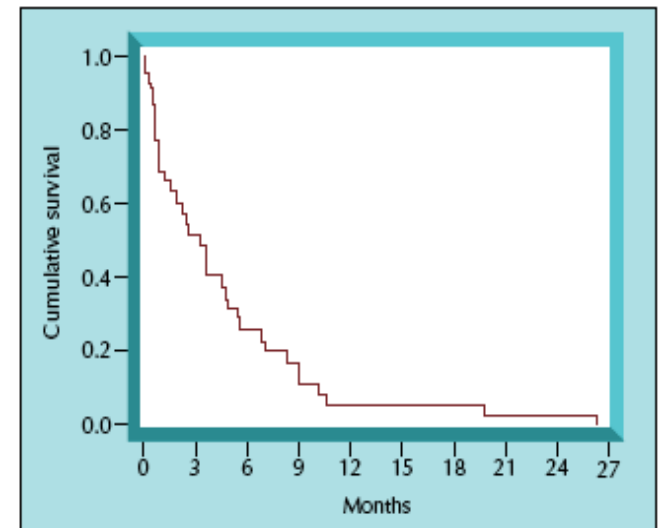
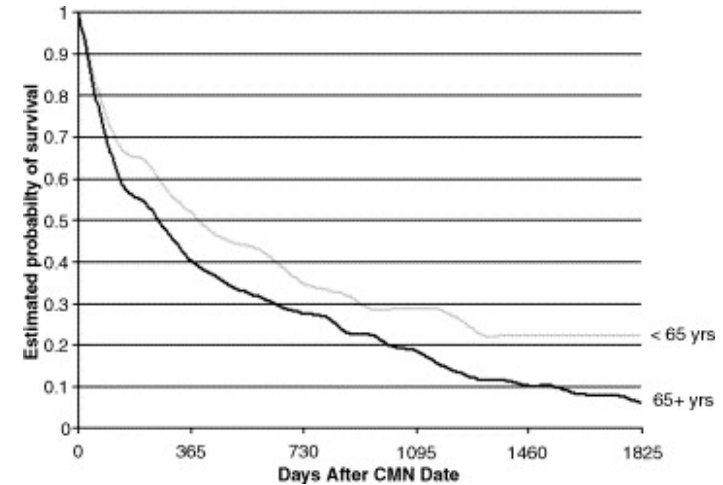
Inotropes as Palliation



Inotropes improve symptoms
50% dead from pump failure by 12 months



No significant difference between
Dobutamine or Milrinone





Summary

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Heart Failure associated with significant morbidity and mortality
Most patients are unaware of this risk

Average heart transplantation survival is now greater than 12 year

LVAD provide durable (5 years +) support

Inotropes improve quality of life, but shortened duration

Decision based on

Medical comorbidities

Right heart hemodynamics

Ability to tolerate anticoagulation

Insurance coverage/Social support

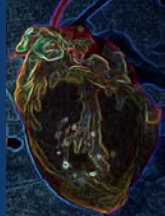
Patient preference

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fedson@bcm.edu





Pathophysiology of Cardiogenic Shock

